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A Diarrhoeic Dog with Clinical and Histopathologic Signs of ICH (*Infectious Canine Hepatitis*)

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Abstract

A 3-month-old male German shepherd dog was referred with depression, vomition, hemorrhagic diarrhea, abdominal pain, anorexia and dehydration. The affected dog did not have any history of vaccination. Despite treatment, the animal died within 2 days after the onset of clinical signs. Gross examination of tissues showed hemorrhages (ecchymoses) in the mucosa of the digestive tract. The liver was congested and slightly enlarged. The gall bladder wall was edematous. The spleen and lymph nodes were also edematous and congested. Light microscopic examination of tissues showed numerous large, basophilic intranuclear inclusion bodies within the hepatcytes and endothelial cells adjacent to the necrotic regions. A large area of hepatic necrosis, severe congestion of sinusoids accompanied by a mild mixed infiltration of inflammatory cells, were evident particularly in the periportal region. Fecal sample was examined for differential diagnosis of other viral, bacterial and parasitic diseases. Based on histopathological findings, *Infectious canine Hepatitis* (ICH) was suspected as the cause of death.

Keywords: Dog, *Infectious Canine Hepatitis*, Pathology

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Introduction

Infectious canine hepatitis (ICH) is an acute liver infection in dogs caused by canine adenovirus type-1 (CAV-1). The virus is spread in the feces, urine, blood, saliva, and nasal discharge of infected dogs. It is contracted through the mouth or nose, where it replicates in the tonsils. The virus then infects the liver and kidneys. The incubation period is 4 to 7 days. Symptoms include fever, depression and loss of appetite, coughing, and a tender abdomen. Corneal edema, kidney disorders (glumerolonephritis) and signs of liver disease such as jaundice, vomiting and hepatic encephalopathy may also occur. Severe cases will develop bleeding disorders, which can cause hematomas to form in the mouth (Sanchez-Cordon *et al.*, 2002; Greene, 2006). Clinical diagnosis may be based on the clinical and pathological findings, which may include moderate to severe leukopenia, neutropenia, lymphopenia and thrombocytopenia. Serum alanine aminotransferase and alkaline phosphatase activities may be increased. Coagulation parameters, PT and PTT are variably affected. Proteinuria (albuminuria) as a reflection of the renal damage caused by the virus can usually be detected. A rising antibody titer to CAV-1 is also seen. The disease can be confused with *canine parvovirus* because both will cause a low white blood cell count and bloody diarrhoea in young, unvaccinated dogs. Treatment is for the symptoms. Prevention is through vaccination. Most combination vaccines for dogs contain a modified canine adenovirus type-1. CAV-1 is destroyed in the environment by steam cleaning and quaternary ammonium compounds. Otherwise, the virus can survive in the environment for months in the right conditions. It can also be released in the urine of a recovered dog for up to a year (Sellon, 2005; Greene, 2006). To the best of our knowledge, this study is the first reported case of ICH suspected dog in Iran.

Case Presentation

A 3-month-old male German shepherd dog was referred to the Veterinary Hospital, Shahid Chamran University of Ahvaz, Southwest of Iran in Spring 2006. The clinical signs were depression, vomiting, haemorrhagic diarrhoea, abdominal pain, anorexia and dehydration. The affected dog did not have any history of vaccination. Blood sample (2 ml) was collected from jugular vein of the affected dog to determine the CBC. He had received supportive treatment for prevention of secondary bacterial infections and correction of dehydration. Fecal sample was examined for other pathogenic bacteria (using culture media), viruses (by immunochromatography assay) and parasites (presence of parasite egg or oocyst). The viral tests were carried out with a commercial rapid Ag test kit (Manufactured by Anigen, Animal genetics, Inc., Korea, 2006), based on the manufacturer's instructions. The kit was a chromatographic immunoassay for the qualitative detection of antigens in samples. The sensitivity and specificity of kits were above 95% (Esfandiari *and* klingeborn 2000). After sudden death, systematic autopsy was performed. Gross and microscopic examinations of different tissues were done.

Results

Despite the treatment, the animal died within 2 days after the onset of clinical signs. The haemogram showed lowered white blood cell count as leukopenia, neutropenia and lymphopenia. Corneal edema and or uveitis were not seen in this case. Gross examination of tissues showed hemorrhages (echymoses) in the mucosa of the digestive tract. The liver was congested and slightly enlarged. The gall bladder wall was edematous. The spleen and lymph nodes were edematous and congested. Light microscopic examination of hematoxylin and eosin stained sections showed numerous large, basophilic intranuclear inclusion bodies within the hepatocytes and endothelial cells. There were metachromatic intranuclear inclusion bodies with chromatin margination (Figs. 1 and 2). A large area of hepatic necrosis, severe congestion in sinusoids

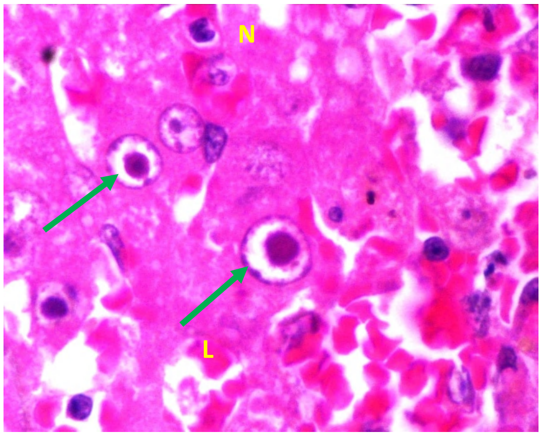


Figure 1: Showing inclusion body in hepatocytes (green arrows). Metachromatic intranuclear inclusion body with chromatin margination, a lymphocyte (L) and one neutrophil (N) have been seen (H&E, × 100).

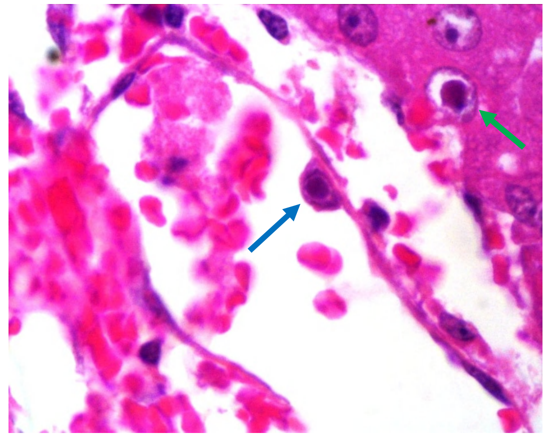


Figure 2: Showing intranuclear inclusion body in the endothelial cell (blue arrow) and hepatocyte (green arrow) (H&E, × 100).

accompanied by a mild lymphocytic and neutrophil infiltration, was evident particularly in the periportal region. Bacteriological culture was negative for significant bacterial pathogens such as *Salmonella*, *Campylobacter*, *Enterotoxigenic Escherichia coli* and *Clostridium perfringens*. The sample was also negative for viruses such as *distemper, parvovirus* and *coronavirus* by immunochromatography assay. There was no parasitic egg or oocyst in fecal samples. ICH was suspected according to histopathological findings.

Discussion

The results of the present case showed that ICH virus must be considered in diarrheic dogs in Iran. Differential diagnosis in a case with bloody diarrhea is very important for proper and quick treatment. There are many stray and rural dogs that are not vaccinated against ICH. These animals can be considered in transmission of the disease to other dogs. Haemorrhagic diarrhea is relatively common in dogs, particularly in rural areas.

In the present case, sudden death was occurred within 2 days after the onset of clinical signs, with no obvious symptoms. The cause of death in ICH is uncertain although the liver is the primary site of viral injury. It may be due to severe organ damage or the development of disseminated intravascular coagulation (DIC). Necropsy findings or biopsy examination of affected tissues in dogs can usually confirm a diagnosis of ICH (Greene, 2006). In the present case, ICH was diagnosed by histopathology.

It has been reported that ICH is most frequently seen in dogs younger than 1 year, although unvaccinated dogs of all ages can be affected (Greene, 2006). In our study, the affected dog was 3-month-old with no history of vaccination. It has been shown that leukopenia and lymphopenia (WBC<6000 cells/µl) is an important paraclinical sign in ICH affected dogs. Although, differential diagnosis of other pathogens is necessary particularly viral enteritis (such as parvovirus, distemper virus and coronavirus). In the present case, differential diagnosis of other pathogens was accomplished by culture (for bacteria), immunochromatography assay (for viruses) and monitoring of feces for parasitic egg or oocyst.

Infectious canine hepatitis was recognized as a specific viral disease of dogs in 1947. The causes of hepatitis in dogs are mostly unknown. Some known causes of canine hepatitis are infectious (CAV-1), toxic (aflatoxin), and metabolic (copper

accumulation). Despite the marked progress in the knowledge on viral causes for human hepatitis, the involvement of infectious agents in the pathogenesis of hepatitis in the dog is still largely unknown. It is very likely that more than one causative infectious agent may cause hepatitis in dogs (Boomkens *et al*., 2004).

The prevalence of ICH varies in different countries. In a report in Italy, four outbreaks of infectious canine hepatitis occurred. Three outbreaks were observed in animal shelters of southern Italy, whereas the fourth outbreak involved two purebred pupies imported from Hungary few days before the onset of clinical symptoms. In all outbreaks canine adenovirus type 1 was identified by virus isolation and PCR. In three outbreaks, other canine viral pathogens were detected, including distemper virus, parvovirus or coronavirus (Decaro *et al*., 2007).

In another survey in Oklahoma University, gross examination of tissues from 2 puppies revealed regionally diffuse hemorrhages in the brain stem and swollen hemorrhagic lymph nodes. Light microscopic examination showed numerous large, basophilic intranuclear inclusion bodies within the central nervous system vascular endothelium and hepatocytes (Caudell *et al*., 2005). An outbreak of dual infection in dogs with canine adenovirus type 1 and canine coronavirus (CCV) infection was reported in an animal shelter that comprised approximately 200 adults' stray dogs and 30 puppies. Twenty puppies died 7-8 days after the onset of the clinical signs. Both CAV-1 and CCV (*Canine Coronavirus*) were isolated from tissue or swab samples (Pratelli *et al*., 2001). 17 cases of cirrhosis and 28 cases of chronic hepatitis with piecemeal necrosis and progressive fibrosis were selected for detection of ICH. Two cases were positive for CAV-1 antigens by the immunoperoxidase method (Chouinard *et al*., 1998). A 72-day-old, female, Golden Retriever dog that had referred with signs including anorexia, coughing, nasal discharge, diarrhea and hematochezia, died on the 15th clinical day. Pathological examination revealed dual infection with *canine distemper virus* (CDV) and *canine adenovirus* (Kobayashi *et al*., 1993).

Diffuse clouding of the cornea (blue eye) of sudden onset and usually transient duration accompanying with anterior uveitis may be attributable to natural infection with canine adenovirus type 1 or to vaccination with live modified virus. It is now recognized that kerato-uveitis is a manifestation of type III hypersensitivity in which immune complex formation resulting from the release of virus, especially from infected corneal endothelial cells, brings corneal endothelial damage and hence corneal edema. At least one breed, the Afghan hound, appears to be particularly susceptible (Greene, 2006). In the present case, corneal edema or uveitis was not seen.

In conclusion, it must be emphasized that vaccination and hygienic procedures are important in the prevention of ICH infection in dog populations. Vaccination against ICH has proved very successful in significantly reducing the incidence of the disease throughout the world. Most vaccines contain attenuated CAV-1 or CAV-2. Recommended vaccination schedules usually begin at about 6 weeks of age and may continue up to 4 months (Sellon, 2005). The present case report showed that CAV-1 is currently circulating in dog population in Iran and vaccination is still required.

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یک مورد سگ اسهالی همراه با علائم بالینی و هیستوپاتولوژی ICH (هپاتیت عفونی سگ ها)

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چکیده

یک قلاده سگ نر ۳ ماهه از نژاد ژرمن شپرد با علائم خمودگی، استفراغ، اسهال هموراژیک، درد شکمی، بی اشتهایی و دهیدراتاسیون ارجاع داده شد. سگ مبتلا، هیچ گونه سابقه واکسیناسیون نداشت. درمان های حمایتی جهت جلوگیری از عفونت های ثانویه و تصحیح دهیدراتاسیون انجام شد. علیرغم درمان، حیوان در طی ۲ روز بعد از شروع علائم بالینی تلف شد. بررسی ماکروسکوپی بافت ها، خونریزی (اکیموز) را در مخاط دستگاه گوارش نشان داد. کبد پرخون و مختصری بزرگ شده بود. کیسه صفرا ادماتوز شده، طحال و عقده های لنفاوی نیز ادماتوز و پرخون بودند. در بررسی هیستوپاتولوژیک بافت ها گنجیدگی های داخل هسته ای بازوفیلیک، متعدد و بزرگ در سلول های کبدی و اندوتلیال نزدیک به نواحی نکروتیک مشاهده گردید. یک ناحیه وسیع از نکروز کبدی، پرخونی شدید در سینوزوئیدها همراه با انتشار خفیف لنفوسیت ها و نوتروفیل ها به ویژه در نواحی اطراف ورید باب دیده شد. نمونه مدفوع برای تشخیص تفریقی سایر بیماری های ویروسی، باکتریایی و انگلی مورد آزمایش قرار گرفت. بر اساس یافته های هیستوپاتولوژیک بیماری هپاتیت عفونی سگ ها (ICH) به عنوان عامل احتمالی مرگ مورد نظر قرار گرفت.

واژگان کلیدی : سگ، هپاتیت عفونی سگ ها، پاتولوژی